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10/567,345	10/31/2006	Jerome Besse	030363-00003	6617

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EXAMINER	
GREENE, IVAN A	

ART UNIT	PAPER NUMBER
1619	

NOTIFICATION DATE	DELIVERY MODE
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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/567,345	BESSE, JEROME	
	Examiner	Art Unit	
	IVAN GREENE	1619	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *31 October 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06 February 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☒ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/31/2006*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of the claims

Claims 1-31 are currently pending and are presented for examination on the merits.

Information Disclosure Statement

The information disclosure statement(s) submitted on 10/31/2006 was filed before the mailing date of the first office action on the merits. The submission is in compliance with the provisions of 37 CFR 1.97. Accordingly, the information disclosure statement has been considered by the Examiner.

Priority

The U.S. effective filing date has been determined to be 08/05/2004, the filing date of the document PCT/FR04/50376. The foreign priority date has been determined to be 08/06/2003, the filing date of document FRANCE 0350403.

Rejections

Claim Rejections - 35 U.S.C. 112 - First Paragraph

1. Claims 10-14 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a Written Description rejection.

M.P.E.P. § 2163 states, "An applicant shows possession of the claimed invention by describing the claimed invention with all of its limitations using such descriptive means as words, structures, figures, diagrams, and formulas that fully set forth the claimed invention…one must define a compound by 'whatever characteristics sufficiently distinguish it'… A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process."

Instant claims 10-14 recite, --derivatives thereof-- for the recited active agents. However, the Specification gives no further description of what, specifically, the "derivative(s)" are. Furthermore, the Specification gives no examples using a "derivative." The skilled artisan cannot readily envision the chemical structure of the claimed subject matter. As such, the instant claims cited above lack adequate written description of "derivatives thereof," as recited in claims 10-14.

Claim Rejections - 35 U.S.C. 112 - Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

1. Claims 1-31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

2. A broad range or limitation together with a narrow range or limitation that falls within the broad range or limitation (in the same claim) is considered indefinite, since the resulting claim does not clearly set forth the metes and bounds of the patent

protection desired. See MPEP § 2173.05(c). Note the explanation given by the Board of Patent Appeals and Interferences in *Ex parte Wu*, 10 USPQ2d 2031, 2033 (Bd. Pat. App. & Inter. 1989), as to where broad language is followed by "such as" and then narrow language. The Board stated that this can render a claim indefinite by raising a question or doubt as to whether the feature introduced by such language is (a) merely exemplary of the remainder of the claim, and therefore not required, or (b) a required feature of the claims. Note also, for example, the decisions of *Ex parte Steigewald*, 131 USPQ 74 (Bd. App. 1961); *Ex parte Hall*, 83 USPQ 38 (Bd. App. 1948); and *Ex parte Hasche*, 86 USPQ 481 (Bd. App. 1949). In the present instance, claim 1 recites the broad recitation dispersible, and the claim also recites orodispersible which is the narrower statement of the range/limitation.

3. Claim 22 is rejected as being indefinite because the claim recites --76,92% in weight of the metformin hydrochloride active ingredient--. It is unclear in what percent the active agent “metformin hydrochloride” should be.

4. Claim 23 is rejected because the claim recites the limitation "metformine chlorhydrate" in line 2. There is insufficient antecedent basis for this limitation in the claim.

5. Claims 24-26 and 28 recite the phrase "preferably." The phrase “preferably” renders the claims indefinite because it is unclear whether the limitation(s) following the phrase are part of the claimed invention. See MPEP § 2173.05(d).

6. Claims 27 is rejected as being indefinite because the claim recites --giving results that can be extrapolated to the compositions of the same type and comprising lower

doses in metformine chlorhydrate, metformine chlorhydrate absorption in human beings, being linear from 0 to 1000 mg--, which is unclear. It is unclear what exactly the limitation of the claim is intended to be and therefore the claim is indefinite.

7. Claim 28 is further rejected because the claim recites the limitation "the metformine chlorhydrate dose" in line 3. There is insufficient antecedent basis for this limitation in the claim.

8. Claim 29 is rejected because the claim recites the limitation "the metformine active" in line 6. There is insufficient antecedent basis for this limitation in the claim.

9. Claim 30 is rejected because the claim recites the limitation "the metformine active" in line 6. There is insufficient antecedent basis for this limitation in the claim.

10. Claim 31 is rejected because the claim recites the limitation "the metformine active" in line 6. There is insufficient antecedent basis for this limitation in the claim.

11. Claims 2-23 are rejected as being dependent from and doing nothing to correct the shortcoming(s) of the parent claim(s).

12. Claims 10-14 are rejected as being indefinite because the claims recite "derivatives for active pharmaceutical ingredients without any further guidance as to what said derivatives are. And as such, the metes and bounds of the claims cannot be determined.

13. Claims 1, 15, 18, 21, are rejected as being indefinite because the claims recite -- under the form of a salt.-- The phrase “under the form of a salt” is confusing when read in the context of the claims and therefore the claims are unclear. The examiner suggests the phrase should read "in the form of a salt."

14. Claims 3-11 and 13 are rejected as being indefinite because the claims recite --agent(s) is (are) selected amongst--. The phrase “agent(s) is (are) selected amongst" is confusing when read in the context of the claims and therefore the claims are unclear. The examiner suggests the phrase should read --agent(s) are selected form the group consisting of--.

15. Claims 1, 2, 15, 17, 18, 21, 22 and 29-31 are rejected as being indefinite because the claims recite --in weight--. The phrase "in weight" is confusing when read in the context of the claims and therefore the claims are unclear. The examiner suggests the phrase should read "by weight."

16. Claim 10 is rejected as being indefinite because in is unclear what the limitation --Glitazone-- is intended to be. The claim recites --a PPAR Gamma agonist...or Glitazone--. Glitazone is a class of drugs and, as such, the phrase should read as "a PPAR Gamma agonist...or a glitazone."

17. Claim 11 is further rejected as being indefinite because it is unclear what the limitation --Glitazar-- is intended to be. The claim recites --characterized in that it comprises, additionally, a PPAR Gamma and Alpha agonist or Glitazar--. The claim language is confusing and “glitazar” is a class of drugs. The examiner suggests the phrase should read as "further comprising a PPAR gamma and alpha agonist or a glitzar selected from the group consisting of."

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

1. Claims 1-28 are rejected under 35 U.S.C. 103(a) as being unpatentable over TIMMINS (US 6,031,004) and BALKAN (US 2003/0139434) as evidenced by TYLER (W.S. TYLER CANADA, product and price catalog).

Applicants Claims

Applicant claims an orodispersible solid pharmaceutical composition having the form of particles with a size lower than 710 µm, containing the metformin active ingredient, characterized in that it comprises: (a) from 65% to 90% in weight of the metformin active ingredient, optionally under the form of a salt, or a combination of the metformin active ingredient with a hypoglycemic active ingredient; (b) from 0.5 to 4% in weight of a binding agent or a combination of binding agents; (c) from 1% to 12% in weight of a disintegrating agent or a combination of disintegrating agents; (d) from 0% to 10% in weight of a diluting agent or a combination of diluting agents; (e) from 0.05%

to 3% in weight of a sweetening agent or a combination of sweetening agents; and (f) one or more additional excipients, the weight percentages being expressed based on the total weight of said composition. Applicant further claims methods of making the pharmaceutical composition which include the steps of mixing and granulating, drying, and compressing into tablets, as well as coating with a sweetening agent.

Determination of the scope

and content of the prior art (MPEP 2141.01)

TIMMINS teaches novel salts of the anti-diabetic agent metformin including metformin fumarate and metformin succinate which may be employed alone or in combination with another anti-hyperglycemic agent (abstract). TIMMINS further teaches the dosage form can be formulated as a tablet or capsule, among others (4:49-52). TIMMINS further teaches the dosage form(s) of their invention may included from about 1% to about 80% of excipients such as lactose, sugar, corn starch, modified corn starch, mannitol, sorbitol, calcium carbonate, and microcrystalline cellulose (5:8-12). TIMMINS further teaches the formulations my comprise one or more binders such as polyvinylpyrrolidone (having a molecular weight of preferably about 40,000), lactose, starches and polyethylene, among others (5:15-23). TIMMINS further teaches disintegrants, such as croscarmellose sodium, crospovidone [cross-linked polyvinylpyrrolidone], sodium starch glycolate, corn starch and microcrystalline cellulose, are included in a preferred amount of about 2% to about 8% by weight (5:24-30). TIMMINS further teaches other excipients such as preservatives, silicon dioxide

and polymeric celluloses (5:34-46). TIMMINS further teaches in examples 9 and 10 the sweetening agent xylitol, and the flavoring agents grape flavor, spice flavor and raspberry flavor (10: 1-35).

TIMMINS teaches the example four (7:29-60) with the following ingredients:

Ingredient	Amount per tablet (mg)
Metformin (2:1) succinate	600.0 mg
Microcrystalline cellulose NF	80.0 mg
Croscarmellose sodium NF	45.0 mg
Hydroxypropylmethyl cellulose (5 cps) (HPMC) USP	15.0 mg
Magnesium Stearate NF	8.0 mg

wherein the active agent metformin succinate is present in an amount of 80% (600/748*100), the binder hydroxypropylmethyl cellulose is present in an amount of 2% (15/748*100), the disintegrant croscarmellose sodium is present in an amount of 6% (45/748*100), the filler/diluting agent microcrystalline cellulose is present in an amount of 10% (80/748*100), and includes the additional excipient magnesium stearate. TIMMINS further teaches the formulation (of example 4) is prepared by wet granulation and includes the steps of mixing, granulating, drying and compressing into tablets (7:45-60).

TIMMINS teaches the additional active ingredients including pioglitazone (3:64), thiazolidinedione [also called glitazone] (4:2), glimepride, glipyride, glipizide, chlorpropamide, gliclazide and acarbose (4:24-26), among others.

Regarding the size of the granules, TIMMINS teaches the mixtures are passed through a #12 to #40 mesh screen (6:3), which according to TYLER indicates a size of 425 microns to 1.7 mm (see TYLER: p. 3, table cols. 1 & 2).

Ascertainment of the difference between

the prior art and the claims (MPEP 2141.02)

The difference between the rejected claims and the teachings of TIMMINS is that TIMMINS does not expressly teach a dipeptidyl peptidase inhibitor and the sugar coating. The deficiencies in the dipeptidyl peptidase inhibitor and the sugar coating are cured by the teachings of BALKAN.

BALKAN teaches combination pharmaceutical compositions which include dipeptidyl peptidase four (DPP-IV) inhibitors and at least one anti-diabetic compound (abstract). BALKAN further teaches the preferred embodiment in which the anti-diabetic compound is selected from metformin, among others ([0150]). BALKAN further teaches the example comprising DPP728 plus metformin ([0175]). BALKAN further teaches the pharmaceutical preparations according to the invention are prepared in a manner known [in the art], for example conventional mixing, granulating, sugar-coating ([0190]). BALKAN further teaches if desired granulating a mixture, and processing the mixture or granules to give tablets or sugar-coated tablet cores ([0190]).

Finding of prima facie obviousness

Rationale and Motivation (MPEP 2142-2143)

It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to combine a DPP-IV inhibitor with a metformin pharmaceutical composition, as suggested by BALKAN, and produce the instantly claimed invention because TIMMINS suggest the use of metformin in combination with another anti-diabetic drug and BALKAN teaches DPP-IV inhibitors as anti-diabetic drugs suitable for use with metformin. One of ordinary skill in the art would have been motivated to combine BALKAN with TIMMINS because formulation produced would have had an increased efficacy by the combination of two anti-diabetic drugs. It would have been obvious to produce a sweetener-coated formulation because the sweetener would have a more appealing taste for the user and increased patient compliance.

From the teachings of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

In light of the forgoing discussion, the Examiner concludes that the subject matter defined by the instant claims would have been obvious within the meaning of 35 USC 103(a).

Conclusion

Claims 1-31 are pending and have been presented for examination on the merits. Claims 1-11, 13, 15, 17, 18, 21, 22, and 29-31 are objected; Claims 10-14 are rejected under 35 U.S.C. 112, first paragraph; claims 1-31 are rejected under 35 U.S.C. 112,

second paragraph; and claims 1-28 are rejected under 35 U.S.C. 103(a). No claims allowed at this time.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to IVAN GREENE whose telephone number is (571)270-5868. The examiner can normally be reached on Monday through Thursday 7AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Johann Richter can be reached on (571) 272-0646. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

IVAN GREENE
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